

Remarks

The objection to the amendment to the specification (Table 4) under 35 U. S. C. 132 as involving new matter, has now been overcome, as suggested by the Office on page 3 of its action, by filing herewith (1) a new written version of the sequence listing that has deleted the objectionable SEQ ID NOS. 121 and 122 from Table 4, (2) a new computer readable disc version of the new written version of the sequence listing, and (3) with the statement that is hereby made, that no new matter is included therein.

Claims 4-6 and 10-14 have been rejected under 35 U.S.C. 112 as indefinite.

These claims have now all been amended, accordingly, to remove each of the matters of indefiniteness raised by the Office.

In claim 4 (and thus also independent claims 5 and 6), it has been made clear that a combination of primer pairs is provided.

All of the criticisms of claim 10 are believed to have been obviated by the present amendment, as follows: reciting the use of all the primer pairs for short distance PCR; rendering the recitation of a BRCA1 gene consistent and with proper antecedent; adopting the language kindly suggested by the Examiner on page 7 of the Office action; lettering the separate method steps and using semi-colons therefore; making clear the exon fragments consistently with the specification; and removing the ambiguity of the word "capable".

Dependent claim 11 has similarly been rendered definite, and also has been amended to delete the phrase "non-detecting".

Claims 12-14 have been rendered definite as to their relation to the method of claim 10.

Withdrawal of the 35 U.S.C 112 indefiniteness rejection of the claims in their present amended form is accordingly believed to be in order and is respectfully requested.

The claims - - all directed and specific to discoveries of specific gene sequences for detecting mutations in BRCA1 genes -- have all been further rejected under 35 U.S.C. 103 upon reference to applicant's own prior patents, even though the Office has had to admit that "Vijg does not teach testing gene sequences of the BRCA1 gene, nor the specific primer pairs of the presently claimed invention".

Nor does the Office find any such teaching of the "the specific primer pairs of the

presently claimed invention" in a single one of, or even any combination of three other references (Park et al., Liskay et al. and Ahern). And yet these references that utterly lack this teaching are supposed to make the present invention "obvious" to an "ordinary artisan"!

Instead, merely because "both Liskay et al and Park et al teach mutations in the BRCA1 gene and its link to cancer", this is supposed to make "the specific primer pairs of the presently claimed invention" somehow "obviously" jump out? And the Ahern article is cited to show an electrophoresis kit of reagents, but certainly not applicant's kits of claims 4-6 or the "specific primer pairs of the presently claimed invention".

The most that the Office offers to try to bolster these clear prior art deficiencies, is the suggestion that "the ordinary artisan would have been motivated to develop primer sequences using the directions of Vijg and routine experimental manipulation". Even if so -- where has the Office demonstrated that these very specific claimed primer sequences result? How this "ordinary artisan" would "obviously" come up with precisely Dr. Vijg's claimed "specific primer pairs of the presently claimed invention" is not explained -- nor is this a tenable or even legal ground of rejection.

It is the duty of the Office to show anticipation -- not just to guess that "routine experimental manipulation" would automatically and obviously lead to "the specific primer pairs of the presently claimed invention" -- which, indeed, eluded the world leader in this field -- the applicant Dr. Vijg himself -- who is certainly far above the "ordinary artisan" postulated by the Office.

This kind of improper "obvious" Sec. 103 rejection was recently condemned by the Federal Circuit (1999) in In re Dembicza, 175 F. 3d 994, 50 U.S.P.Q. 2d 1614:

"the insidious effect of a hindsight syndrome where that which only the inventor taught is used against the teacher".

The J. Med Genet 1999 article of Dr. Vijg submitted with the preliminary amendment of August 2, 2002, moreover, shows the totally unexpected result as claimed by applicant's "specific primer pairs of the presently claimed invention". The specific and novel sequences of applicant, indeed, lead to the discovery of "an additional five (mutations) that had previously escaped detection" with prior BRCA1 detection systems!

The abstract also discloses that

"in addition to the 19 mutations, a total of 15 different polymorphic variance were

scored most of which were recurring".

This was thus hardly "obvious".

In view of the difficulty applicant has been experiencing with trying to satisfy the Office with acceptable claim language, applicant specifically submits claims 15,16 and 17 as another possibly acceptable approach, just referencing the contents of the tables herein.

Reconsideration and allowance are accordingly in order and are respectfully requested.

Any costs required by this filing, included for any required extensions of time, petition for which is hereby made, may be charged to account 18-1425 of the undersigned counsel.

Respectfully submitted,

RINES AND RINES

Date: April 11, 2003
Rines and Rines
81 North State Street
Concord, N.H. 03301
Reg. No. 15,932
Tel. (603) 228-0121

By: Robert H. Rines
Robert H. Rines,
Attorney for Applicant
Reg. No. 15932

Table 4

EXON FRAGMENT	PRIMER SEQUENCES	CLAMPING SEQUENCE (S)	TARGET LENGTH	MELTING TEMP. (°C)
2	2F - SEQ ID NO: 79 2R - SEQ ID NO: 80	SEQ ID NO: 29 SEQ ID NO: 31	203	34.64
3	3F - SEQ ID NO: 81 3R - SEQ ID NO: 82	SEQ ID NO: 31 SEQ ID NO: 27	269	37.22
5	5F - SEQ ID NO: 83 5R - SEQ ID NO: 84	SEQ ID NO: 27 SEQ ID NO: 31	305	26.69
6	6F - SEQ ID NO: 85 6R - SEQ ID NO: 86	NO CLAMP	213	35.52
7	7F - SEQ ID NO: 87 7R - SEQ ID NO: 88	NO CLAMP	250	32.67
8	8F - SEQ ID NO: 89 8R - SEQ ID NO: 90	NO CLAMP	248	40.51
9	9F - SEQ ID NO: 91 9R - SEQ ID NO: 92	NO CLAMP	242	24.26
10	10F - SEQ ID NO: 93 10R - SEQ ID NO: 94	SEQ ID NO: 27 NO CLAMP	229	38.3
11.1	11.1F - SEQ ID NO: 47 11.1R - SEQ ID NO: 48	SEQ ID NO: 30	347	40.99
11.2	11.2F - SEQ ID NO: 49 11.2R - SEQ ID NO: 50	SEQ ID NO: 31	461	40.74
11.3	11.3F - SEQ ID NO: 51 11.3R - SEQ ID NO: 52	NO CLAMP	438	35.04
11.4	11.4F - SEQ ID NO: 53 11.4R - SEQ ID NO: 54	SEQ ID NO: 31	475	34.85
11.5	11.5F - SEQ ID NO: 55 11.5R - SEQ ID NO: 56	SEQ ID NO: 32	468	33.66
11.6	11.6F - SEQ ID NO: 57 11.6R - SEQ ID NO: 58	SEQ ID NO: 30	410	40.51
11.7	11.7F - SEQ ID NO: 59 11.7R - SEQ ID NO: 60	NO CLAMP	345	36.45
11.8	11.8F - SEQ ID NO: 61 11.8R - SEQ ID NO: 62	NO CLAMP	365	38.37

o



Table 4 continued

EXON.FRAGMENT	PRIMER SEQUENCES	CLAMPING SEQUENCE(S)	TARGET LENGTH	MELTING TEMP. (°C)
11.9	11.9F-SEQ ID NO: 63 11.9R - SEQ ID NO: 64	SEQ ID NO: 30 SEQ ID NO: 27	422	40.4
11.10	11.10F-SEQIDNO: 65 11.10R - SEQ ID NO: 66	SEQIDNO:31 SEQ ID NO: 29	292	35.93
11.11	11.11F-SEQ ID NO: 67 11.11R - SEQ ID NO: 68	SEQ IDNO:29 NO CLAMP	390	33.06
11.12	11.12F - SEQ ID NO: 69 11.12R - SEQ ID NO: 70	SEQ ID NO: 31 SEQ ID NO: 29	309	33.22
11.13	11.13F-SEQIDNO: 71 11.13R - SEQ ID NO: 72	SEQ ID NO: 29 NO CLAMP	305	37.43
11.14	11.14F - SEQ ID NO: 73 11.14R - SEQ ID NO: 74	SEQ ID NO: 29 SEQ ID NO: 31	378	43.03
11.15	11.15F - SEQ ID NO: 75 11.15R - SEQ ID NO: 76	NO CLAMP	460	39.33
11.16	11.16F-SEQ ID NO: 77 11.16R - SEQ ID NO: 78	SEQ ID NO: 27	356	44
12	12F - SEQ ID NO: 95 12R - SEQ ID NO: 96	SEQ ID NO: 27 SEQ ID NO: 30	289	48.54
13	13F - SEQ ID NO: 97 13R - SEQ ID NO: 98	SEQ ID NO: 27 SEQ ID NO: 30	293	45.18
14	14F - SEQ ID NO: 99 14R - SEQ ID NO: 100	SEQ ID NO: 27 SEQ ID NO: 30	417	30.78
15	15F - SEQ ID NO: 101 15R - SEQ ID NO: 102	SEQ ID NO: 29	303	46.07
16	16F - SEQ ID NO: 103 16R - SEQ ID NO: 104	SEQ ID NO: 29	427	47.49
17	17F - SEQ ID NO: 105 17R - SEQ ID NO: 106	SEQ ID NO: 27 SEQ ID NO: 32	242	32.51
18	18F - SEQ ID NO: 107 18R - SEQ ID NO: 108	SEQ ID NO: 31 SEQ ID NO: 27	194	36.32
19	19F - SEQ ID NO: 109 19R - SEQ ID NO: 110	NO CLAMP SEQ ID NO: 27	178	32.32

Table 4 Continued

EXON FRAGMENT	PRIMER SEQUENCES	CLAMPING SEQUENCE (S)	TARGET LENGTH	MELTING TEMP. (°C)
20	20F - SEQ ID NO: 111 20R - SEQ ID NO: 112	SEQ ID NO: 27 NO CLAMP	219	46.4
21	21F- SEQ ID NO: 113 21R - SEQ ID NO: 114		172	49.95
22	22F - SEQ ID NO: 115 22R - SEQ ID NO: 116	SEQ ID NO: 27 SEQ ID NO: 30	209	47.71
23	23F - SEQ ID NO: 117 23R - SEQ ID NO: 118	SEQ ID NO: 31 SEQ ID NO: 27	275	49.47
24	24F - SEQ ID NO: 119 24R - SEQ ID NO: 120		325	59.79